

WHAT IS CLAIMED IS:

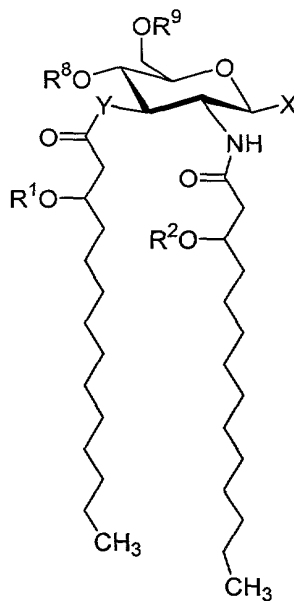
1. An immunostimulant composition comprising:

(a) at least one aminoalkyl glucosaminide phosphate (AGP); and

(b) at least one saponin.

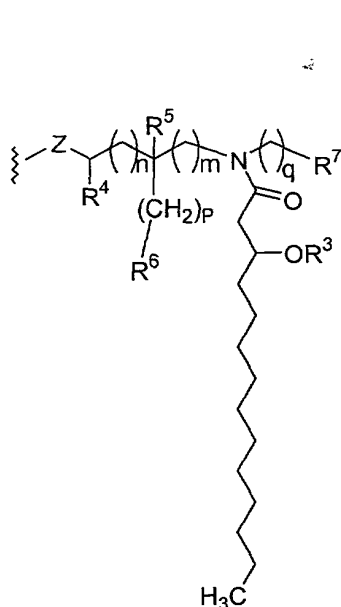
2. The composition of claim 1, wherein the AGP comprises a compound

having the structure:

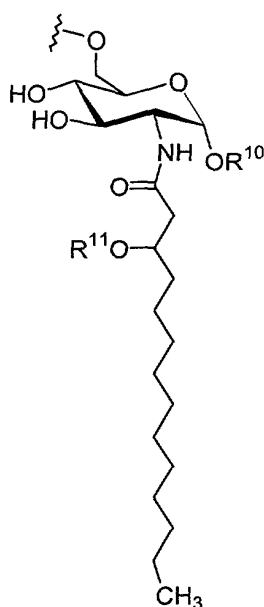


(I)

and pharmaceutically acceptable salts and derivatives thereof, wherein Y is $-O-$ or $-NH-$; R^1 and R^2 are each independently selected from saturated and unsaturated (C_2-C_{24}) aliphatic acyl groups; R^8 is $-H$ or $-PO_3R^{11}R^{12}$, wherein R^{11} and R^{12} are each independently $-H$ or (C_1-C_4) aliphatic groups; R^9 is $-H$, $-CH_3$ or $-PO_3R^{13}R^{14}$, wherein R^{13} and R^{14} are each independently selected from $-H$ and (C_1-C_4) aliphatic groups; and wherein at least one of R^8 and R^9 is a phosphorus-containing group, but R^8 and R^9 are not both phosphorus-containing groups; and X is a group selected from the formulae:

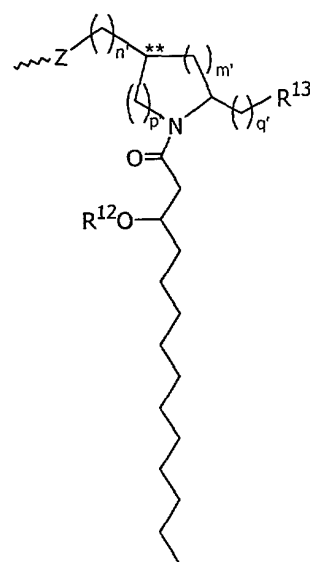


(Ia)



(Ib)

and



(Ic)

wherein the subscripts n, m, p, q, n', m', p' and q' are each independently an integer of from 0 to 6, provided that the sum of p' and m' is an integer from 0 to 6; R³, R¹¹, and R¹² are independently a saturated or unsaturated optionally substituted aliphatic (C₂-C₂₄)acyl group, provided that when X is formula (Ia), one of R¹, R² and R³ is optionally hydrogen; R⁴ and R⁵ are independently selected from H and methyl; R⁶ and R⁷ are independently selected from H, OH, (C₁-C₄)oxyaliphatic groups, -PO₃H₂, -OPO₃H₂, -SO₃H, -OSO₃H, -NR¹⁵R¹⁶, -SR¹⁵, -CN, -NO₂, -CHO, -CO₂R¹⁵, -CONR¹⁵R¹⁶, -PO₃R¹⁵R¹⁶, -OPO₃R¹⁵R¹⁶, -SO₃R¹⁵ and -OSO₃R¹⁵, wherein R¹⁵ and R¹⁶ are each independently selected from H and (C₁-C₄)aliphatic groups; R¹⁰ is selected from H, CH₃, -PO₃H₂, ω-phosphonooxy(C₂-C₂₄)alkyl, and ω-carboxy(C₁-C₂₄)alkyl; R¹³ is independently selected from H, OH, (C₁-C₄)oxyaliphatic groups, -PO₃R¹⁷R¹⁸, -OPO₃R¹⁷R¹⁸, -SO₃R¹⁷, -OSO₃R¹⁷, -NR¹⁷R¹⁸, -SR¹⁷, -CN, -NO₂, -CHO, -CO₂R¹⁷, and -CONR¹⁷R¹⁸, wherein R¹⁷ and R¹⁸ are each independently selected from H and (C₁-C₄)aliphatic groups; and Z is -O- or -S-.

- 34 3 The composition of claim 2, wherein X is a group of formula (Ia).
35
36 4. The composition of claim 2, wherein X is a group of formula (Ib).
37
38 5. The composition of claim 2, wherein X is a group of formula (Ic).
39
40 6. The composition of claim 2, wherein X is formula (Ia) and one of R¹,
41 R² and R³ is hydrogen.
42
43 7. The composition of claim 2, wherein R¹, R², R³, R¹¹ and R¹² are each
44 acyl.
45 8. The composition of claim 3, wherein R¹, R² and R³ are each C₇-C₁₆
46 aliphatic acyl groups.
47
48 9. The composition of claim 3, wherein R¹, R² and R³ are each C₈-C₁₄
49 aliphatic acyl groups.
50
51 10. The composition of claim 3, wherein R¹, R² and R³ are each C₉-C₁₄
52 aliphatic acyl groups.
53
54 11. The composition of claim 3, wherein R¹, R² and R³ are each C₁₀-C₁₄
55 aliphatic acyl groups.
56
57 12. The composition of claim 3, wherein R¹, R² and R³ are each C₁₀-C₁₄
58 saturated aliphatic acyl groups.
59
60 13. The composition of claim 5, wherein R¹, R² and R¹² are each C₉-C₁₄
61 aliphatic acyl groups.
62
63 14. The composition of claim 5, wherein R¹, R² and R¹² are each C₁₀-C₁₄
64 aliphatic acyl groups.
65
66 15. The composition of claim 5, wherein R¹, R² and R³ are each C₁₀-C₁₄
67 saturated aliphatic acyl groups.

- 68
- 69 16. The composition of claim 2, wherein X is oxygen.
- 70
- 71 17. The composition of claim 2, wherein R⁸ is a phosphorus-containing
- 72 group and R⁹ is hydrogen.
- 73
- 74 18. The composition of claim 2, wherein R⁸ or R⁹ is a phosphorus-
- 75 containing group, and R¹¹ and R¹², or R¹³ and R¹⁴, respectively, are both hydrogen.
- 76
- 77 18. The composition of claim 3, wherein the total of $n + m$ is 0, 1, or 2.
- 78
- 79 19. The composition of claim 3, wherein p and q are independently 0, 1 or
- 80 2.
- 81 20. The composition of claim 3, wherein R⁶ is selected from hydrogen,
- 82 hydroxy and carboxy.
- 83
- 84 21. The composition of claim 5, wherein n' , m' , p' and q' are independently
- 85 0, 1 or 2.
- 86
- 87 22. The composition of claim 5, wherein n' is 1, m' is 2, and p' and q' are
- 88 zero.
- 89 23. The composition of claim 22, wherein R¹, R² and R¹² are each C₁₀-C₁₄
- 90 saturated aliphatic acyl groups.
- 91
- 92 24. The composition of claim 23, wherein Y and Z are both oxygen; R¹³ is
- 93 hydrogen; and R¹, R² and R¹² are each C₁₀ saturated aliphatic acyl groups.
- 94
- 95 25. The composition of claim 23, wherein Y and Z are both oxygen; R¹³ is
- 96 hydrogen; and R¹, R² and R¹² are each C₁₂ saturated aliphatic acyl groups.
- 97
- 98 26. The composition of claim 23, wherein Y and Z are both oxygen; R¹³ is
- 99 hydrogen; and R¹, R² and R¹² are each C₁₄ saturated aliphatic acyl groups.
- 100

27. The composition of claim 1, wherein the AGP is a monophosphoryl lipid A.

28. The composition of claim 3, wherein R^1 , R^2 and R^3 all are $n\text{-C}_{13}\text{H}_{27}\text{CO}$; X and Y are both oxygen; n , m , p , and q are each zero; R^4 , R^5 , R^6 , R^7 and R^9 are each hydrogen; and R^8 is PO_3H_2 .

29. The composition of claim 3, wherein R^1 , R^2 and R^3 all are $n\text{-C}_{11}\text{H}_{23}\text{CO}$; X and Y are both oxygen; n , m , and q are each zero; p is 1; R^4 , R^5 , R^7 and R^9 are each hydrogen; R^6 is hydroxy; and R^8 is PO_3H_2 .

30. The composition of claim 1 wherein the saponin is selected from naturally obtained saponins, synthetically obtained saponins, saponin conjugates, saponin derivatives, and saponin mimetics.

31. The composition of claim 1, wherein the saponin comprises a Quillaja saponin.

32. The composition of claim 31, wherein the Quillaja saponin comprises Quil A, QS-7, QS-17, QS-18 or QS-21.

33. The composition of claim 1, wherein the saponin comprises a triterpene saponin-lipophile conjugate comprising a nonacylated or desacylated triterpene saponin that includes a 3-glucuronic acid residue; and a lipophilic moiety; wherein said saponin and said lipophilic moiety are covalently attached to one another, either directly or through a linker group, and wherein said direct attachment or attachment to said linker occurs through a covalent bond between the carboxyl carbon of said 3-glucuronic acid residue and a suitable functional group on the lipophilic residue or linker group.

34. The composition of claim 33, wherein the triterpene saponin (a) has a triterpene aglycone core structure with branched sugar chains attached to positions 3 and 28, and an aldehyde group linked or attached to position 4; and (b) is either originally non-acylated, or requires removal of an acyl or acyloyl group that is bound to a saccharide at the 28-position of the triterpene aglycone

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15 34. The composition of claim 33, wherein said lipophilic moiety comprises
16 one or more residues of a fatty acid, terpenoid, aliphatic amine, aliphatic alcohol, aliphatic
17 mercapton mono- or poly- C₂-C₄ alkyleneoxy derivative of a fatty acid, mono- or poly- C₂-C₄
18 alkyleneoxy derivative of a fatty alcohol, glycosyl-fatty acid, glycolipid, phospholipid or a
19 mono-, or di-acylglycerol.

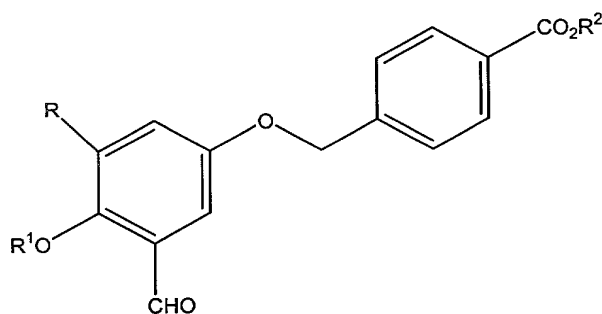
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21 35. The composition of claim 1, wherein the saponin comprises GPI-0100.
22

23 36. The composition of claim 33, wherein said triterpene saponin has a
24 quillaic acid or gypsogenin core structure.

1 37. The composition of claim 36, wherein said desacylsaponin or
2 nonacylated saponin is selected from the group consisting of Quillaja desacylsaponin, S.
3 jennisensis desacylsaponin Gypsophila saponin, Saponaria saponin Acanthophyllum saponin
4 and lucyoside P saponin.

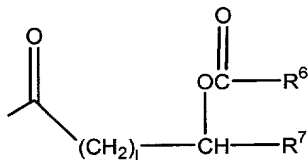
1 38. The composition of claim 1, wherein the saponin comprises a
2 saponin/antigen covalent conjugate composition.

1 39. The composition of claim 1, wherein the saponin comprises a
2 compound represented by the formula:



3
4 wherein, R is hydrogen or $-\text{C}(\text{O})\text{H}$; R^1 is a member selected from the group
5 consisting of hydrogen, an optionally substituted C₁₋₂₀ aliphatic group, a saccharyl
6 group, and a group represented by the formula $-\text{C}(\text{O})-[\text{C}(\text{R}^3)(\text{R}^4)]_k-\text{COOH}$, wherein
7 each R^3 and R^4 independently is a member selected from the group consisting of
8 hydrogen and optionally substituted C₁₋₁₀ aliphatic groups, and k is a number from 1

to 5; R² is a member selected from the group consisting of hydrogen, an optionally substituted C₁₋₂₀ aliphatic group, and a group represented by the formula
 $-(CH_2)_rCH(OH)(CH_2)_tOR^5$, wherein r and t are independently 1 or 2, and R⁵ is an optionally substituted C₂₋₂₀ aliphatic group, or a group represented by the formula



wherein j is 1-5, and R⁶ and R⁷ are independently selected from the group consisting of hydrogen and optionally substituted C₁₋₂₀ aliphatic groups; or a pharmacologically acceptable salt thereof.

40. The composition of claim 39, wherein R¹ is a mono- or disaccharide.

41. The composition of claim 40, wherein R¹ is a glucuronic acid group.

42. The composition of claim 39, wherein R, R¹ and R² are hydrogens.

43. The composition of claim 39, wherein R is hydrogen; R¹ is a saccharyl group, wherein the saccharyl group is a glucuronic acid group; and R² is hydrogen.

44. The composition of claim 39, wherein R is hydrogen; R¹ is represented by the formula $-C(O)-[C(R^3)(R^4)]_k-COOH$ wherein R³ and R⁴ are hydrogens and k is 2; and R² is hydrogen.

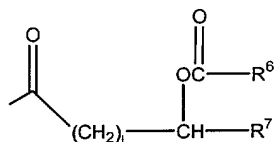
45. The composition of claim 39, wherein R is hydrogen; R¹ is a saccharyl group, wherein the saccharyl group is a glucuronic acid group; and R² is $(CH_2)_rCH(OH)(CH_2)_tOR^5$, wherein r and t are both 1, and R⁵ is an optionally substituted C₂₋₂₀ acyl group.

46. The composition of claim 43, wherein the glucuronic acid group is a β-D-glucuronic acid group.

47. The composition of claim 45, wherein $(CH_2)_rCH(OH)(CH_2)_tOR^5$ is a 1-O-acyl-*sn*-glyceryl group.

48. The composition of claim 47, wherein R⁵ is a member selected from the group consisting of acetyl, octanoyl, and tetradecanoyl groups.

1 49. The composition of claim 39, wherein R is hydrogen; R¹ is a saccharyl
2 group, wherein the sachharyl group is a glucuronic acid group; and R² is a group represented
3 by the formula:



4
5 wherein j is 1; R⁶ is an optionally substituted C₁₋₂₀ aliphatic group; and R⁷ is an
6 optionally substituted C₁₋₂₀ aliphatic group.

1 50. The composition of claim 49, wherein R⁷ is an optionally substituted
2 C₁₁ aliphatic group.

1 51. The composition of claim 1, further comprising at least one antigen.

1 52. The composition of claim 51, wherein the antigen is derived from the
2 group consisting of Herpes Simplex Virus type 1, Herpes Simplex virus type 2, Human
3 cytomegalovirus, HIV, Hepatitis A, B, C or E, Respiratory Syncytial virus, human papilloma
4 virus, Influenza virus, Tuberculosis, Leishmaniasis, T.Cruzi, Ehrlichia, Candida, Salmonella,
5 Neisseria, Borrelia, Chlamydia, Bordetella, Plasmodium and Toxoplasma.

1 53. The composition of claim 51, wherein the antigen is a human tumor
2 antigen.

1 54. The composition of claim 53, wherein the tumor antigen is derived
2 from a prostate, colon, breast, ovarian, pancreatic, brain, head and neck, melanoma, leukemia
3 or lymphoma cancer.

1 55. The composition of claim 51, wherein the antigen is a self antigen.

1 56. The composition of claim 55, wherein the self antigen is an antigen
2 associated with an autoimmune disease.

1 57. The composition of claim 52, wherein the autoimmune disease is type
2 1 diabetes, multiple sclerosis, myasthenia gravis, rheumatoid arthritis or psoriasis.

1 58. The composition of claim 1 comprising an aqueous formulation.

1 59. The composition of claim 58, wherein the aqueous formulation
2 comprises one or more surfactants.

1 60. The composition of claim 59, wherein the aqueous formulation
2 comprises one or more phospholipid surfactants.

1 61. The composition of claim 60, wherein the surfactant is selected from
2 the group consisting of diacyl phosphatidyl glycerols, diacyl phosphatidyl cholines, diacyl
3 phosphatidic acids, and diacyl phosphatidyl ethanolamines.

1 62. The composition of claim 60, wherein the surfactant is selected from
2 the group consisting of dimyristoyl phosphatidyl glycerol (DPMG), dipalmitoyl phosphatidyl
3 glycerol (DPPG), distearoyl phosphatidyl glycerol (DSPG), dimyristoyl phosphatidylcholine
4 (DPMC), dipalmitoyl phosphatidylcholine (DPPC), distearoyl phosphatidylcholine (DSPC);
5 dimyristoyl phosphatidic acid (DPMA), dipalmitoyl phosphatidic acid (DPPA), distearoyl
6 phosphatidic acid (DSPA); dimyristoyl phosphatidyl ethanolamine (DPME), dipalmitoyl
7 phosphatidyl ethanolamine (DPPE) and distearoyl phosphatidyl ethanolamine (DSPE).

1 63. The composition of claim 1, comprising an emulsion formulation.

1 64. The composition of claim 1, comprising a solid formulation.

1 65. The composition of claim 1, wherein the AGP and saponin are present
2 in synergistically effective amounts.

1 66. The composition of claim 1, wherein the saponin and AGP are present
2 in a weight ratio of saponin:AGP of from about 1000:1 to about 1:1000.

1 67. The composition of claim 1 further comprising a vaccine.

1 68. The composition of claim 2, wherein the saponin is selected from
2 naturally obtained saponins, synthetically obtained saponins, saponin conjugates, saponin
3 derivatives, and saponin mimetics.

1 69. The composition of claim 3, wherein the saponin is a quillaja saponin.

- 8
- 9 70. The composition of claim 69, wherein the saponin is QS-21.
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- 11 71. The composition of claim 3, wherein the saponin is a saponin-lipophile
- 12 conjugate.
- 13
- 14 72. The composition of claim 71, wherein the saponin is GPI-0100.
- 15
- 16 73. The composition of claim 4, wherein the saponin is a quillaja saponin.
- 17
- 18 74. The composition of claim 73, wherein the saponin is QS-21.
- 19
- 20 75. The composition of claim 4, wherein the saponin is a saponin-lipophile
- 21 conjugate.
- 22
- 23 76. The composition of claim 75, wherein the saponin is GPI-0100.
- 24
- 25 77. The composition of claim 24, wherein the saponin is QS-21.
- 26
- 27 78. The composition of claim 24, wherein the saponin is GPI-0100.
- 28
- 29 79. The composition of claim 25, wherein the saponin is QS-21.
- 30
- 31 80. The composition of claim 25, wherein the saponin is GPI-0100.
- 32
- 33 81. The composition of claim 26, wherein the saponin is QS-21.
- 34
- 35 82. The composition of claim 26, wherein the saponin is GPI-0100.
- 36
- 37 83. The composition of claim 27, wherein the saponin is a quillaja saponin.
- 38
- 39 84. The composition of claim 83, wherein the saponin is QS-21.
- 40

85. The composition of claim 27, wherein the saponin is a saponin-lipophile conjugate.

86. The composition of claim 85, wherein the saponin is GPI-0100.

87. A method of treating a mammal suffering from or susceptible to a pathogenic infection, cancer or an autoimmune disorder comprising administering to the mammal an effective amount of a composition according to claim 1.

88. A method of treating a mammal suffering from or susceptible to a pathogenic infection, cancer or an autoimmune disorder comprising administering to the mammal an effective amount of a composition according to claim 2

89. A method of treating a mammal suffering from or susceptible to a pathogenic infection, cancer or an autoimmune disorder comprising administering to the mammal an effective amount of a composition according to claim 30.

90. A method of enhancing the immune response in an animal which comprises administering to the animal a composition according to claim 1.

91. A method of enhancing the immune response in an animal which comprises administering to the animal a composition according to claim 2.

92. A method of enhancing the immune response in an animal which comprises administering to the animal a composition according to claim 30.

93. A method of enhancing the immune response in an animal to an antigen which comprises administering to the animal a composition according to claim 1 in combination with an antigen.

94. A method of enhancing the immune response in an animal to an antigen which comprises administering to the animal a composition according to claim 2 in combination with an antigen.

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95. A method of enhancing the immune response in an animal to an

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antigen which comprises administering to the animal a composition according to claim 30 in

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combination with an antigen.

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